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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/405,050	09/27/1999	YEHUDA SHOENFELD	ZAP-1CIPCONC	9070

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EXAMINER
NAVARRO, ALBERT MARK

ART UNIT	PAPER NUMBER
1645	19

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/405,050	Applicant(s) Shoenfield et al
	Examiner Mark Navarro	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-11 and 22-29* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3, 6-11, and 22-29* is/are rejected.

7) ☒ Claim(s) *4 and 5* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's response filed on November 7, 2002 has been received and entered. Consequently claims 1-11 and 22-29 are pending in the instant application.

Claim Rejections - 35 USC § 102

1. The rejection of claims 1-2, 7-9, and 25-28 under 35 U.S.C. 102(b) as being anticipated by Chapel *et al* is maintained.

Applicant's are asserting that the Examiner's argument assumes that the patients in Chapel et al had metastatic lymphoma, i.e., the lymphoma was of a type that was capable of metastasizing or was in fact metastasizing, and was therefore subject to "inhibition of metastasis" through administration of IVIG as defined in the instant application. Applicant's further assert that the non-Hodgkin's lymphoma described in Chapel et al could have been metastatic or non-metastatic - each scenario is possible and plausible. Applicant's assert that if there was no metastasis present or none capable of occurring, then no inhibition of metastasis can have taken place at the time of IVIG administration, and no inherent anticipation can have occurred, because each of the rejected claims requires the inhibition of metastasis or treatment of metastatic lymphoma.

Applicant's arguments have been fully considered but are not found to be fully persuasive.

First, Chapel et al disclose the administration of IVIG to patients with non-Hodgkin's lymphoma. Applicant's are respectfully directed to the claim language. Claim 1: A method for inhibiting metastasis of lymphoma in a mammal which comprises administering to the mammal a

preparation of IVIG or fragments thereof selected from the group consisting of $F(ab')_2$, Fab', Fab and Fc.

Applicant's assert that the Examiner has assumed that the patients in Chapel et al had metastatic lymphoma. However, contrary to Applicant's summary of the Examiner's position, no such assumption has been made. Again looking at the claim, mammals with lymphoma receive IVIG. Chapel et al disclose of mammals with lymphoma receiving IVIG. It is the administration of IVIG which is responsible for the "inhibition of metastasis." Given that Chapel et al disclose that mammals with lymphoma received IVIG, each and every single one of them underwent "inhibition of metastasis." It is not germane whether the non-Hodgkins lymphomas reported in Chapel were actively metastasizing or even capable of metastasizing, each and every one of them was "inhibited" from metastasizing simply by the administration of IVIG.

Applicant's further assert that if there was no metastasis present or none capable of occurring, then no inhibition of metastasis can have taken place at the time of IVIG administration. However, first, the claims do not require determining if the non-Hodgkins lymphoma displays metastatic potential, second, the inhibition occurs as a result of IVIG administration, which is exactly what Chapel et al did. In a nut shell, even mammals with non metastasizing non-Hodgkins lymphoma were "inhibited" from metastasizing by the administration of IVIG. The fact of whether or not metastasis occurred or could have potentially occurred is irrelevant, in view that in each scenario, metastasis is inhibited because of the presence of IVIG.

Applicant's have additionally cited *Rapoport v. Dement*, 59 USPQ2d 1215, 1222 (Fed. Cir. 2001) that "the mere fact that a certain thing may result from a given set of circumstances is not sufficient." However, nothing has been established using probabilities or possibilities. As set forth above each mammal with a lymphoma had its metastatic potential inhibited simply by receiving IVIG as claimed.

Chapel *et al* (Clin. Res. 1988, 36(3) page 407A) disclose of patients with low grade non-Hodgkin's lymphoma receiving intravenous immunoglobulins. (See abstract).

In view that patients with lymphoma received IVIG as claimed, the result of inhibiting metastasis of the lymphoma is deemed to be an inherent result of the administered IVIG, and consequently anticipates the claimed invention.

For reasons of record in Paper Number 16, as well as the above cited reasons this rejection is maintained.

2. The rejection of claims 1-3, 7-11, 25 and 28 under 35 U.S.C. 102(b) as being anticipated by Morell *et al* is maintained.

Applicant's assertions are essentially the same as those set forth above in paragraph 1, and have been addressed accordingly above in paragraph 1.

Morell *et al* (Pediatr. Infect Dis. J. Vol. 7, No. 5, pp S87-S91, 1988) disclose of 9 patients who were on cytostatic therapy for non-Hodgkin's lymphoma receiving 0.4g/kg of IVIG

daily. Morell *et al* further set forth that of administering IVIG for greater than 5 consecutive days. (See page S90 and Figure 3).

In view that patients with lymphoma received IVIG in an amount of 2g/kg/month as claimed, the result of inhibiting metastasis of the lymphoma is deemed to be an inherent result of the administered IVIG, and consequently anticipates the claimed invention.

For reasons of record in Paper Number 16, as well as the above cited reasons this rejection is maintained.

3. The rejection of claims 1-3, 6-9, and 25-28 under 35 U.S.C. 102(b) as being anticipated by Besa *et al* is maintained.

Applicant's assertions are essentially the same as those set forth above in paragraph 1, and have been addressed accordingly above in paragraph 1.

Besa *et al* (American Journal of Medicine Apr. 1988, Vol. 84(4), pp 691-698) disclose of patients with Hodgkin's lymphoma and non-Hodgkin's lymphoma treated with intravenous immunoglobulin (0.4g/kg) daily for five doses followed by maintenance therapy every 21 to 28 days if evidence of recurrence was noted. (See abstract).

In view that patients with lymphoma received IVIG in an amount of 2g/kg/month as claimed, the result of inhibiting metastasis of the lymphoma is deemed to be an inherent result of the administered IVIG, and consequently anticipates the claimed invention.

For reasons of record in Paper Number 16, as well as the above cited reasons this rejection is maintained.

4. The rejection of claim 29 under 35 U.S.C. 102(b) as being anticipated by Vitetta *et al* is maintained.

Applicant's are asserting that Vitetta et al disclose the use of the Fab' fragment of a monoclonal anti-CD22 antibody coupled to chemically deglycosylated ricin A chain, and that this is not an IVIG as defined in Applicants' specification.

Applicant's arguments have been fully considered but are not found to be fully persuasive.

Applicant's are again respectfully directed to the claims, IVIG is not required for claim 29. Claim 29 recites administering a preparation of fragments of IVIG selected from the group consisting of $F(ab')_2$, Fab', Fab and Fc. Vitetta et al disclose of a Fab' fragment, the exact fragment required by the claims. Furthermore, Applicant's define IVIG as "gamma globulin preparations suitable for intravenous use, **such as** those IVIG preparations commercially available from several sources. (Emphasis added). Clearly the Fab' fragment disclosed by Vitetta et al is suitable for intravenous use, since it was administered to patients. Consequently, each and every claim limitation has been addressed.

Vivetta *et al* (Cancer Research Vol. 51, pp 4052-4058, August 1, 1991) disclose of Fab' fragments attached to ricin A chain being administered to patients with refractory B-cell lymphomas. (See abstract).

In view that Vivetta *et al* disclose of the intravenous administration of Fab' fragments to a mammal with a B-cell lymphoma, the disclosure of Vivetta *et al* is deemed to anticipate the claimed invention.

For reasons of record in Paper Number 16, as well as those recited above, this rejection is maintained.

Double Patenting

5. The rejection of claims 1-11 and 22-29 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 5,965,130 is maintained.

Applicant's have indicated a willingness to filed a terminal disclaimer to overcome this rejection, however until a terminal disclaimer is filed and made of record, this rejection is maintained for reasons of record in Paper Number 16.

6. The rejection of claims 1-11 and 22-29 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 5,562,902 is maintained.

Applicant's have indicated a willingness to filed a terminal disclaimer to overcome this rejection, however until a terminal disclaimer is filed and made of record, this rejection is maintained for reasons of record in Paper Number 16.

Claim Rejections - 35 USC § 112

7. The rejection of claims 22-29 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "method for treating" is maintained.

Applicant's are asserting that "treating" is a commonly used word with an ordinary meaning that would have been known to one of skill in the art of the filing date of the application. Applicant's assert that the American Heritage Dictionary defines "treat" as to give medical aid to counteract (a disease or condition).

Applicant's arguments have been fully considered but are not found to be fully persuasive.

Using Applicant's supplied dictionary, what is being counteracted? (i.e., inhibition of metastasis, tumor regression, reduction of pain, amelioration of symptoms?) Without a clear idea of what is being counteracted the metes and bounds of treatment cannot be defined by one of skill in the art.

Claims 4-5 are objected to as depending upon a rejected base claim, however claims 4-5 are free of the prior art of record.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro, whose telephone number is (703) 306-3225. The examiner can be reached on Monday - Thursday from 8:00 AM - 6:00 PM. The examiner can be reached on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Lynette Smith can be reached at (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1645 by facsimile transmission. Papers should by faxed to Group 1645 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703) 308-4242.

Mark Navarro

Primary Examiner

January 23, 2003